Citation:

Chung BH, Cho BH, Liang P, Doran S, Osterlund L, Oster RA, Darnell B, Franklin F. Contribution of postprandial lipemia to the dietary fat-mediated changes in endogenous lipoprotein-cholesterol concentrations in humans. *Am J Clin Nutr.* 2004 Nov; 80(5): 1,145-1,158.

PubMed ID: 15531660

Study Design:

Randomized crossover trial.

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine if dietary fat alters endogenous lipoprotein cholesterol and cardiovascular disease (CVD) risk by affecting the potency and rate of post-prandial triacylglycerol-rich lipoproteins (TRLs) to carry cholesterol accepted from endogenous low density lipoprotein (LDL) and high density lipoprotein (HDL) and from cell membranes via lecithin:cholesterol acyltransferase (LCAT) and cholesterol ester transfer protein (CETP) to the liver for its removal by examining the acute and chronic effects of consuming a diet rich in polyunsaturated fatty acids (PUFA) or saturated fatty acids (SFA).

Inclusion Criteria:

Healthy normolipidemic men and post-menopausal women.

Exclusion Criteria:

Based on a brief physical exam and review of medical history, subjects were excluded if:

- Fasting triacylglycerol concentration was above 75th percentile
- Plasma cholesterol was above 95th percentile
- HDL was below 10th percentile
- Taking any medication
- Reporting unusual diet habits (vegetarian, heavy drinker, etc.).

Description of Study Protocol:

Recruitment

Healthy normolipidemic men and post-menopausal women were recruited to participate in the

study on a voluntary basis.

Design

Randomized crossover trial:

- Subjects adopted each of two diets for a 20-day period, allowing a three- to four-week ad libitum period in between
- Meals, prepared by the research center, contained 15% energy from protein, 50% energy from carbohydrate and 35% energy from fat, and had 175mg cholesterol per 1,000kcal
- PUFA-rich diet provided 7.5% SFAs, 12% monounsaturated fatty acids (MUFA), 15.5% PUFA
- SFA-rich diet provided 18.8% SFA, 11.5% MUFA, and 4.7% PUFA
- Fat-loading study meals were done on day 16 and 20
- Fasting and post-prandial blood samples were collected immediately before the meal and both four hours and seven hours after the meal.

Intervention

All subjects participated in both interventions due to cross-over design.

Statistical Analysis

- Utilized mean ± standard deviation, mixed models, ANOVA and Tukey's multiple comparisons test
- All tests were two-sided and performed at a 5% significance level using the SAS software (version 9.0, SAS Institute Ince, Cary, NC).

Data Collection Summary:

Timing of Measurements

- Day 1: Entry date (before starting either diet)
- Day 16: After consuming PUFA or SFA diet
- Day 20: Challenge day to assess reaction to quick change
- Three to four weeks ad libitum diet between study periods.

Dependent Variables

- Plasma triglyceride (TG)
- Plasma total cholesterol (C)
- Plasma unesterified cholesterol (UC)
- Plasma cholesteryl ester (CE)
- VLDL-C
- LDL-C
- HDL-C
- TRL-C.

Independent Variables

- PUFA diet for 20 days
- SFA diet for 20 days.

Control Variables

Subjects served as own controls.

Description of Actual Data Sample:

- *Initial N:* 16 participants (8 males, 8 females)
- *Attrition (final N):* None; 16 completed the trial
- *Age:* Males 33 to 49 years (mean 35.3±4.5); females 45 to 62 years (mean 51.9±6.6)
- *Ethnicity:* Males (seven white, one black); females (five white, three black)
- *Anthropometrics:* Body Mass Index (kg/m^2) for males was 25.3±4.1; females 29.6±4.5
- *Location:* Alabama, US.

Summary of Results:

Key Findings:

- PUFA-rich diet significantly decreased total cholesterol and CE due to a significant reduction in LDL (-12.3%, P<0.05) with no significant reduction in HDL (-3.8%, NS)
- SFA-rich diet caused no significant change in total cholesterol and CE or either LDL or HDL
- Neither diet significantly affected triacylglycerol, UC or VLDL
- Post-prandial clearance (in vivo) of cholesterol was greater with a PUFA diet than a SFA diet.

The table below indicates the changes in lipids and lipoproteins on Day 1 and Day 16 of both of the test diets (units in mmol per liter).

	PUFA Day 1	PUFA Day 16	SFA Day 1	SFA Day 16
TG	1.07±0.43	1.03±0.43	1.06±0.39	1.12±0.45
C	4.61±1.06	4.22±1.06	4.64±0.96	4.81±1.01
UC	1.06±0.21	1.01±0.20	1.02±0.23	1.04±0.22
CE	3.56±0.89	3.20±0.92	3.62±0.85	3.78±0.97
VLDL	0.29±0.20	0.32±0.20	0.31±0.22	0.34±0.22
LDL	2.94±0.93	2.59±0.86	2.99±0.89	3.07±0.91
HDL	1.37±0.41	1.32±0.38	1.34±0.37	1.40±0.34

Polyunsaturated Fatty Acid (PUFA), Saturated Fatty Acid (SFA), Plasma Triglyceride (TG), Plasma total cholesterol (C), Plasma unesterified cholesterol (UC), Plasma cholesteryl ester (CE), Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL).

Other Findings

- The appearance of post-prandial TRLs in plasma at four hours was linked to a significant lowering of both LDL (-7.4%) and HDL (-4.8%) after a PUFA-rich diet; no such effect was observed after the SFA-rich diet
- The appearance of post-prandial TRLs in plasma increased the cholesteryl ester transfer protein-mediated transfer of cholesteryl ester from LDL + HDL to TRLs in vitro without a significant influence from dietary fat.

Author Conclusion:

The induction of post-prandial lipemia after both PUFA- and SFA-rich diets resulted in a significant increase in TRL cholesterol and triacylglycerol and concomitant transient decrease in LDL and HDL cholesterol. The clearance rate of post-prandial TRLs is influenced by dietary fat composition with chronic PUFA-rich diet leading for faster clearance rate and SFA-rich diet leading to slower clearance rate. The clearance rate of post-prandial TRLs may play an important role in regulating fasting plasma cholesterol concentrations and thus the risk of CVD.

Reviewer Comments:

Meals provided by research center for specific content, thorough discussion of laboratory procedures. Small sample size and recruitment methods were not described. Relatively short period of diet intake to assess change; potential impact of participant intake between diet phases was not discussed.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes